UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,571	06/26/2003	Richard P. Batycky	2685.2046 US3	6287

38421 7590 10/29/2010

ELMORE PATENT LAW GROUP, PC
515 Groton Road
Unit 1R
Westford, MA 01886

EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
10/29/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RICHARD P. BATYCKY, GIOVANNI CAPONETTI, MARIKO CHILDS, ELLIOT EHRICH, KAREN FU, JEFFREY S. HRKACH, WEN-I LI, MICHAEL M. LIPP, MEI-LING PAN, and JASON SUMMA

Appeal 2010-002312
Application 10/607,571
Technology Center 1600

Before CAROL A. SPIEGEL, LORA M. GREEN, and MELANIE L. McCOLLUM, *Administrative Patent Judges*.

McCOLLUM, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to an epinephrine administration method and epinephrine-containing particles.

---

[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm-in-part.

STATEMENT OF THE CASE

Claims 140-143, 146-150, 153, 156-170, 172, and 173 are on appeal (App. Br. 2). Claim 171 is also pending but has been indicated to be allowable (Ans. 2). We will focus on claims 140 and 172, which read as follows:

140. A method for administering epinephrine to a patient in need of epinephrine, the method comprising:

administering spray-dried particles from a dry powder inhaler to the respiratory system of the patient in a single, breath-activated step, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient;

wherein the particles administered to the patient comprise at least about 50 micrograms of epinephrine, have a tap density of less than 0.4 g/cm^3 and possess a fine particle fraction of less than 5.6 microns of at least about 45 percent.

172. Particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) about 11 to about 21 weight percent epinephrine bitartrate;

(b) about 62 to about 82 weight percent leucine; and

(c) about 7 to about 17 weight percent sodium tartrate.

The other claims discussed herein are set forth in the "Claims Appendix" to the Appeal Brief (App. Br. 31-34).

Claims 140-143, 153, and 156-160 stand rejected under 35 U.S.C. § 103(a) as obvious over Tarara[2] in view of Slutsky[3] (Ans. 3).

---

[2] Tarara et al., US 2005/0074498 A1, Apr. 7, 2005.
[3] Slutsky et al., US 6,102,036, Aug. 15, 2000.

Claims 161 and 162 stand rejected under 35 U.S.C. § 103(a) as obvious over Tarara in view of Slutsky and Physician's Desk Reference (hereinafter "PDR") (Ans. 8).

Claims 163-170 stand rejected under 35 U.S.C. § 103(a) as obvious over Tarara in view of Slutsky and Warren[4] (Ans. 13).

Claims 140-143, 146-150, 159, 160, and 162 stand rejected under 35 U.S.C. § 103(a) as obvious over Foster[5] in view of Tarara and Slutsky (Ans. 10).

Claims 172 and 173 stand rejected under 35 U.S.C. § 103(a) as obvious over Foster in view of Tarara, Slutsky, and Drug Information Handbook (hereinafter "DIH") (Ans. 15).

PRINCIPLES OF LAW

> [I]t is elementary that the mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.

In re Best, 562 F.2d 1252, 1254-55 (CCPA 1977). "Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, on 'prima facie obviousness'

---

[4] J.B. Warren et al., *Systemic absorption of inhaled epinephrine*, 40 CLIN. PHARMACOL. THER. 673-678 (1986).
[5] Foster et al., US 2003/0215512 A1, Nov. 20, 2003.

under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same." *Id.* at 1255.

"[I]t is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456 (CCPA 1955).

"Attorney's argument in a brief cannot take the place of evidence." *In re Pearson*, 494 F.2d 1399, 1405 (CCPA 1974).

I

The Examiner rejects claims 140-143, 153, and 156-160 as obvious over Tarara in view of Slutsky, claims 161 and 162 as obvious over Tarara in view of Slutsky and PDR, and claims 163-170 as obvious over Tarara in view of Slutsky and Warren (Ans. 3-10 & 13-14).

The Examiner relies on Tarara for disclosing particles having the features recited in claim 140 (*id.* at 4-6). The Examiner relies on Slutsky for teaching "a breath activated inhaler, which may contain a single dose of a powdered medicament, which is intended to be inhaled by the patient in a single breath," and a "breath-activated inhaler capable of delivering a large dose of powdered medicament in a single breath" (*id.* at 6).

The Examiner concludes that it would have been obvious "to combine the teachings of Tarara and Slutsky, because as taught by Slutsky, use of Slutsky's invented inhaler would allow one to deliver a large dose in a single breath" (*id.* at 7). Regarding the amount of epinephrine delivered, the Examiner concludes:

> The combination of Tarara's invented compositions with Slutsky's invented inhaler would reasonably be expected to deliver at least 50 micrograms of epinephrine, because one can modify the dosage of epinephrine present in an inhaler to ensure the delivery of a therapeutically effective amount of

> epinephrine and Slutsky's inhaler permits delivery of an entire dose in a single breath.

(*Id.*)

Issue

Does the evidence support the Examiner's obviousness rejections of claims 140-143, 153, and 156-170 over Tarara and Slutsky, alone or in view of PDR or Warren?

Findings of Fact

1. The Specification discloses:

> The terms "FPF(<5.6)," "FPF(<5.6 microns)," and "fine particle fraction of less than 5.6 microns" as used herein, refer to the fraction of a sample of particles that have an aerodynamic diameter of less than 5.6 microns. FPF(<5.6) can be determined by dividing the mass of particles deposited on the stage one and on the collection filter of a two-stage collapsed [Andersen Cascade Impactor (ACI)] by the mass of particles weighed into a capsule for delivery to the instrument.

(Spec. 35.)

2. The Specification also discloses:

> Suitable inhalers which are single, breath-actuated inhalers that can be employed in the methods of the invention include but are not limited to simple, dry powder inhalers disclosed in U.S. Patents 4,995,385 and 4,069,819, Spinhaler® (Fisons, Loughborough, U.K.), Rotahaler® (GlaxoSmithKline, Research Triangle Technology Park, North Carolina), FlowCaps® (Hovione, Loures, Portugal), Inhalator® (Boehringer-Ingelheim, Germany), Aerolizer® (Novartis, Switzerland), Diskhaler® (GlaxoSmithKline, RTP, NC), Diskus® (GlaxoSmithKline, RTP, NC) and others, such as known to those skilled in the art.

(*Id.* at 57.)

3. Tarara discloses particles in the form of a dry powder "for the delivery of a bioactive agent to the respiratory tract of a patient" (Tarara, Abstract).

4. Tarara also discloses that "the particles may be used in conjunction with an inhalation device such as a dry powder inhaler [DPI], metered dose inhaler [MDI] or a nebulizer" (*id.*).

5. In addition, Tarara discloses that the powder may comprise an excipient (*id.* at ¶ [0040]).

6. Tarara also discloses that "particularly preferred embodiments typically comprise perforated microstructures formed by spray drying" (*id.* at ¶ [0075]).

7. In addition, Tarara discloses:

> [F]or highly active materials the perforated microstructures may incorporate as little as 0.001% by weight [active or bioactive agent] although a concentration of greater than about 0.1% w/w is preferred. Other embodiments of the invention may comprise greater than about 5%, 10%, 15%, 20%, 25%, 30% or even 40% w/w active or bioactive agent. Still more preferably the perforated microstructures may comprise greater than about 50%, 60%, 70%, 75%, 80% or even 90% wIw [sic] active or bioactive agent. The precise amount of active or bioactive agent incorporated in the perforated microstructures of the present invention is dependent upon the agent of choice, the required dose, and the form of the agent actually used for incorporation. Those skilled in the art will appreciate that such determinations may be made by using well-known pharmacological techniques in combination with the teachings of the present invention.

(*Id.* at ¶ [0068].)

8. Tarara also discloses that exemplary bioactive agents include adrenaline, i.e., epinephrine (*id.* at ¶ [0070]).

9. In addition, Tarara discloses that "the density of the particles is significantly less than 1.0 g/cm^3, typically less than 0.5 g/cm^3, more often on the order of 0.1 g/cm^3, and as low as 0.01 g/cm^3" (*id.* at ¶ [0126]).

10. In Examples X-XIII, Tarara discloses particles having a tap density of less than 0.1 g/cm^3 (*id.* at ¶¶ [0276]-[0290]).

11. Tarara also discloses: "[T]he mean aerodynamic diameter of the perforated microstructures is preferably less than about 5 μm, more preferably less than about 3 μm, and, in particularly preferred embodiments, less than about 2 μm. Such particle distributions will act to increase the deep lung deposition of the bioactive agent." (*Id.* at ¶ [0126].)

12. In addition, Tarara discloses:

> As used herein the phrase "fine particle fraction" refers to the percentage of the total amount of active medicament delivered per actuation from the mouthpiece of a DPI, MDI or nebulizer onto plates 2-7 of an 8 stage Andersen cascade impactor. Based on such measurements the formulations of the present invention will preferably have a fine particle fraction of approximately 20% or more by weight of the perforated microstructures (w/w), more preferably they will exhibit a fine particle fraction of from about 25% to 80% w/w, and even more preferably from about 30 to 70% w/w. In selected embodiments the present invention will preferably comprise a fine particle fraction of greater than about 30%, 40%, 50%, 60%, 70% or 80% by weight.

(*Id.* at ¶ [0127].)

13. Tarara also discloses:

> [T]he two major types of DPIs comprise unit dose delivery devices and bulk reservoir delivery systems. . . . Currently, the range of dry powder that can be filled into a unit dose container

> is in the range of 5 to 15 mg which corresponds to drug loading in the range of 25 to 500 µg per dose. . . . Currently bulk reservoir type DPIs can meter between 200 µg to 20 mg powder per actuation.

(*Id.* at ¶ [0132].)

14. Slutsky states:

> There are a number of problems with pressurized[, that is, self-propelled,] aerosols. Pressurized aerosols require coordination on the part of the user who ideally should inhale at exactly the same time as the device is actuated in order to deliver the drug into the lungs. . . . In addition, even if the user properly aims the delivery device and coordinates the inhalation, the speed with which the aerosol is expelled from the device and enters the mouth causes much of the aerosol to impact on the throat and upper airways of the user.

(Slutsky, col. 2, ll. 46-62 & 33-35.)

15. Slutsky therefore discloses a "method of assisting a person to withdraw from cigarette induced nicotine dependency, comprising introducing a predetermined dose of a non-pressurized, particulate medicament comprising at least one nicotine formulation . . . into a breath activated inhaler" (*id.* at Abstract).

16. Slutsky also discloses that the "predetermined dose of nicotine may be from about 0.1 to about 10 mg" (*id.* at col. 3, ll. 46-48).

17. In addition, Slutsky discloses a breath activated inhaler "contain[ing] a single dose of a medicament which is intended to be inhaled by the patient in a single breath" (*id.* at col. 4, ll. 47-49).

18. Slutsky also discloses that "a large dose of medicament may be inhaled in a single breath" (*id.* at col. 12, ll. 51-52).

19. In addition, Slutsky discloses that breath activated inhalers are generally known in the art (*id.* at col. 6, ll. 16-23).

20. Slutsky also discloses:

> Most inhalers currently in use for the treatment of respiratory disorders use a low resistance so that sufficient air flow can be generated by persons having impeded respiratory capacity and obstructed airways, resulting, for example, from asthmatic attack. However, the high flow rates generated by users not having obstructed airways could cause the fine particles of the medicament to impact against the back of the upper airway. Accordingly, *one embodiment of the present invention* provides an inhalation device with a resistor . . . to restrict the cross-sectional area of the air conduit so as to reduce the flow rate of air thereby decreasing impaction at the back of the throat.

(*Id.* at col. 7, ll. 14-26 (emphasis added).)

Analysis

Tarara discloses a method comprising administering spray-dried particles from a dry powder inhaler to the respiratory system of a patient, the particles comprising a bioactive agent and an excipient (Findings of Fact (FF) 3-6). Tarara also discloses using adrenaline as the bioactive agent and particles having a tap density of less than 0.4 g/cm^3 (FF 8 & 10). Slutsky discloses administering a dose of medicament in a single, breath-activated step (FF 15 & 17-18).[6] We agree with the Examiner that it would have been obvious to administer Tarara's particles in a single, breath-activated step (Ans. 7).

[6] In addition, Appellants admit that "single, breath-actuated inhalers that can be employed in the methods of the invention" were known in the art (FF 2).

Appellants argue, however, that there is "[n]o reason to select epinephrine and assume efficient delivery in a single breath actuated inhaler" (App. Br. 11). In particular, Appellants argue that, "[a]t best, if one were to attempt delivering epinephrine to a patient according to the teachings of Tarara, one would select the preferred MDIs or a propellant actuated bulk reservoir DPIs" (*id.*). We are not persuaded.

Appellants have not presented evidence supporting this position. On the contrary, the evidence of record indicates that there are problems associated with self-propelled inhalers, which would have led one of ordinary skill in the art to select a breath-activated inhaler (FF 14).

Appellants also argue:

> One skilled in the art would not be motivated to combine Slutsky's inhaler which is intended to restrict the flow rate of large doses of nicotine to a healthy breather with a therapeutic such as epinephrine for delivery to a person who may be having difficulty breathing and wherein relief in as little as a single breath is essential.

(App. Br. 12). We are not persuaded.

The Examiner concludes that an "ordinary skilled artisan would have been motivated to utilize an inhaler capable of delivering a therapeutically effective dose in a single breath . . . because one would need fewer administrations to deliver a therapeutically effective dose contained in an inhaler" (Ans. 7). Even if it would not have been obvious to use a breath-activated inhaler that restricts the flow rate, as described in one embodiment of Slutsky (FF 20), we agree with the Examiner that it would have been obvious to utilize a breath-activated inhaler that has not be modified to restrict the flow rate.

In addition, Appellants argue that "Tarara teaches the need for ten to twenty actuations for success, not high FPFs in a single breath" (App. Br. 7). In particular, Appellants argue:

> The Examiner has provided no basis for concluding that Tarara provides a generic teaching that a unit dose container in a DPI which may contain from 5 to 15 mg teaches the desirability and means to deliver at least 50 micrograms of epinephrine (or any other drug) to a patient in need thereof in a *single breath-activated step* at the stated *fine particle fraction less than 5.6 microns*.

(*Id.*) Appellants also argue that the math in Tarara's examples and specification does not add up and the Examiner erroneously believes that it is appropriate to ignore this date (*id.* at 8-11). We are not persuaded.

Tarara discloses that "the range of dry powder that can be filled into a unit dose container is in the range of 5 to 15 mg which corresponds to drug loading in the range of 25 to 500 µg per dose" and that "bulk reservoir type DPIs can meter between 200 µg to 20 mg powder per actuation" (FF 13). Whether or not Tarara's proprietary dry powder inhaler (DPI) can be used to administer at least 50 µg of epinephrine in a single, breath-activated step, we agree with the Examiner that it would have been obvious to do so in view of the teachings of Slutsky (Ans. 7). Slutsky discloses that "a large dose of medicament may be inhaled in a single breath" (FF 18). In particular, Slutsky discloses a nicotine dose of from about 0.1 to about 10 mg (FF 16). Based on these disclosures, we agree with the Examiner that there is a reasonable expectation for success in administering at least 50 µg of epinephrine in a single, breath-activated step (Ans. 7).

With regard to the claimed fine particle fraction, the Specification defines the term "fine particle fraction of less than 5.6 microns" as "the fraction of a sample of particles that have an aerodynamic diameter of less than 5.6 microns" (FF 1). Tarara discloses that "the mean aerodynamic diameter of the perforated microstructures is preferably less than about 5 μm, more preferably less than about 3 μm, and, in particularly preferred embodiments, less than about 2 μm" (FF 11). In addition, Tarara teaches that a high fine particle fraction is desirable (FF 12). Based on these disclosures, we agree with the Examiner that Tarara suggests powder in which at least 45% of the particles have an aerodynamic diameter of less than 5.6 microns. Although we recognize that the present Specification determines the fine particle fraction somewhat differently that Tarara (FF 1 & 12), we do not agree with Appellants that this difference or any miscalculations in Tarara's examples renders the claimed fine particle fraction non-obvious.

Furthermore, Appellants' argument that they "do not believe that a person of skill in the art would assume that a single breath activated inhalation (which generally applies less dispersion energy) will be equivalent to or exceed a propellant-based inhaler after 20 actuations" (Reply. Br. 4) misses the point. The rejection is not based on any assumption that a single breath activated inhalation will be equivalent to or exceed a propellant-based inhaler after 20 actuations. Instead, the rejection is based on the prima facie obviousness of using Tarara's powder in Slutsky's inhaler (Ans. 7). Appellants have not provided evidence that this combination provides unexpectedly superior results.

With regard to claims 142-143, Appellants additionally argue that "Tarara does not teach the selection of 1 to 45% and 1 to 30% (respectively) by weight of epinephrine" (App. Br. 15). We are not persuaded. Instead, we agree with the Examiner that Tarara discloses amounts that broadly encompass the claimed ranges (FF 7) and that claimed amounts of epinephrine would have been prima facie obvious based on this disclosure (Ans. 19).

With regard to claim 153, Appellants additionally argue that "Tarara does not teach the selection of a powder that contains about 250 micrograms to about 5 milligrams of epinephrine" (App. Br. 15). We are not persuaded. Instead, we agree with the Examiner that Tarara discloses "drug loading in the range of 25 to 500 μg per dose" (FF 13) and that claimed amounts of epinephrine would have been prima facie obvious based on this disclosure (Ans. 19).

With regard to claims 156-160, Appellants argue that "Tarara does not teach the selection of a powder that is designed to deliver epinephrine to the upper airways (Claim 158), alveoli (Claim 157) or both (Claim 156) and the corresponding ability to target systemic (Claim 159) or local (Claim 160) activity" (App. Br. 15). In response, the Examiner argues:

> [T]he teachings of Tarara reasonably suggest powder formulations comprising epinephrine and characterized by the same and/or overlapping physical parameters (i.e. average particle size, tap density, and FPF). As a consequence, it is only logical that the inhalation administration of these powder formulations will necessarily result in delivery to approximately the same locations within the respiratory tract and have the same or similar systemic and/or local effects.

(Ans. 20.) We conclude that the Examiner has set forth a reasonable basis to shift the burden to Appellants to demonstrate that the combination of Tarara with Slutsky would not necessarily result in the features of claims 156-160. Appellants have not met this burden.

With regard to claims 161-162, the Examiner relies on PDR for teaching the additional features of these claims (Ans. 8-9). Appellants argue that PDR does not overcome the deficiencies in Tarara and Slutsky discussed above (App. Br. 16). However, we are not persuaded by this argument for the reasons discussed above.

With regard to claims 163-170, the Examiner additional relies on Warren (Ans. 13). The Examiner finds that "Warren's teachings . . . support the notion that administration of Tarara's compositions comprising epinephrine as the active agent using Slutsky's single breath-actuated inhaler would necessarily yield the same or substantially similar pharmacokinetic results as are articulated in Appellants' claims" (Ans. 26). In particular, the Examiner finds:

> because the teachings of Tarara fairly suggest a powder composition comprising epinephrine and having the required properties of claim 140 it follows that the inhalation administration of Tarara's suggested composition would necessarily exhibit the same or substantially similar Cmax properties when compared to the Cmax resulting from the administration of epinephrine using a liquid-based (e.g. aqueous) aerosol.

(*Id.* at 27.) We conclude that the Examiner has set forth a reasonable basis for the inherency position and Appellants have not adequately explained why this position is in error.

Conclusion

The evidence supports the Examiner's obviousness rejections of claims 140-143, 153, and 156-170 over Tarara and Slutsky, alone or in view of PDR or Warren. We therefore affirm these rejections.

II

The Examiner rejects claims 140-143, 146-150, 159, 160, and 162 as obvious over Foster in view of Tarara and Slutsky (Ans. 10-12).

The Examiner relies on Foster for disclosing particles having many of the features of claim 140 (*id.* at 10-11). The Examiner acknowledges, however, that "Foster lacks the teaching of compositions having a tap density of less than 0.4 g/cm^3," but finds that Tarara cures this deficiency (*id.* at 12). The Examiner relies on Slutsky as discussed above (*id.* at 10).

The Examiner concludes:

> It would have been obvious to a person of ordinary skill in the art at the time of the instant application to combine the teachings of Foster and Tarara/Slutsky, because all inventors teach compositions suitable for inhalation pulmonary administration of active agents. A skilled artisan would have been motivated to combine the teachings of Foster and Tarara, because Tarara's compositions provide teachings of desirable physical characteristics of aerodynamically light particles especially suitable for inhalation administration. An ordinary skilled artisan cognizant of the teachings of Slutsky would be motivated to utilize Slutsky's breath-activated inhaler to improve patient compliance and facilitate delivery of a particulate pharmaceutical formulation in the fewest number of administrations.

(*Id.* at 12.)

Appellants argue:

> [W]hile both Tarara and Foster provide compositions "suitable for inhalation" as asserted by the Examiner, the compositions disclosed in each reference are no more alike then an antibody composition and a small molecule composition that may both be "suitable for injection". The Examiner has not articulated *how* one would combine the teachings of Foster and Tarara, retaining the important features of each, and thereby provide a composition suitable for inhalation with the Slutsky inhaler.

(App. Br. 18.)

Issue

Has the Examiner set forth a prima facie case that it would have been obvious to combine Foster with Tarara?

Findings of Fact

21. Foster "relates to powdered pharmaceutical compositions that exhibit improved stability of dispersibility over time for inhalation therapy" (Foster ¶ [0003]).

22. Foster discloses "a powdered, dispersible composition . . . compris[ing] a mixture of a pharmaceutically-acceptable glassy matrix and at least one pharmacologically active material within the glassy matrix" (*id.* at ¶ [0017]).

23. Foster defines the term "powder" as "a composition that consists of finely dispersed solid particles that are substantially free flowing and capable of being readily dispersed in an inhalation device and subsequently inhaled by a subject so that the particles reach the lungs to permit penetration into the alveoli" (*id.* at ¶ [0044]).

Analysis

The Examiner acknowledges that "Foster lacks the teaching of compositions having a tap density of less than 0.4 g/cm^3" (Ans. 12). Although Tarara discloses particles having this tap density (FF 10), we agree with Appellants that the Examiner has not adequately explained how Foster is being combined with Tarara to provide the claimed particles.

Conclusion

The Examiner has not set forth a prima facie case that it would have been obvious to combine Foster with Tarara. We therefore reverse the obviousness rejection over Foster, Tarara, and Slutsky of claim 140 and of claims 141-143, 146-150, 159, 160, and 162, which depend from claim 140.

III

The Examiner rejects claims 172 and 173 as obvious over Foster in view of Tarara, Slutsky, and DIH (Ans. 15-17).

The Examiner relies on Foster for disclosing "a composition that comprises a mixture of a pharmaceutically acceptable glassy matrix and at least one pharmacologically active material within the glassy matrix" (*id.* at 10). The Examiner finds that the "unit dosage typically will be between 0.25 mg and 15 mg of total material in the dry powder, wherein the active will comprise about 0.05% to about 99.0% by weight of the composition [0054]," that "[a]ctive small molecules . . . for use in Foster's compositions include . . . adrenaline [0056]," that "the most preferable glass formers include sodium tartrate . . . [0071] to [0072]," and that "the composition may contain other additives (i.e. excipients) [0064], including non-polar amino acids (e.g. leucine) [0068]" (Ans. 10-11).

The Examiner relies on Tarara and Slutsky as discussed above (*id.* at 15). The Examiner relies on DIH for disclosing the use of epinephrine bitartrate (*id.*). The Examiner concludes that it would have been obvious "to combine the teachings of Tarara/Foster with the DIH" (*id.* at 16).

With regard to the claimed amounts, the Examiner finds:

> Foster teaches an overlapping range for the amount [of active agent] (i.e. about 0.05% to about 99.0% by w/w). In addition, it would have been readily apparent to a skilled artisan per the teachings of Foster that the remainder of the composition would comprise glass-forming excipient (i.e. sodium tartrate) and other additives (e.g. leucine). The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of Appellants' invention.

(*Id.*)

Appellants argue: "[T]he claims require the addition of a large amount of leucine. Leucine is not disclosed as a preferred excipient (or 'additive') and there is no guidance in [Foster] which would suggest that it would be desirable to select leucine and add it in a large quantity." (App. Br. 26.) On the contrary, Appellants argue that Foster "suggests that such 'additives' should be added in an amount less than 20% w/w" (*id.* at 26-27).

Issue

Has the Examiner set forth a prima facie case that the applied references suggest particles comprising about 62 to about 82 weight percent leucine?

Findings of Fact

24. Foster discloses that, "[i]n addition to the glass former excipient, other additives may be included to aid in stability of the active, adjust the pH (i.e. a buffering agent), improve dispersibility, aid in providing uniformity of delivery, and other purposes" (Foster ¶ [0064]).

25. Foster also discloses that suitable additives include amino acids, such as leucine (*id.* at ¶ [0068]).

26. In addition, Foster discloses:

> [T]he pharmacologically active material will be present in an amount that will range between about 0.05% w for a drug that is very active to about 99% w for a drug that is not very active and is a glass former itself. Generally, the range of active drug will be from about 0.2% w to about 97.0% w, preferably about 0.5% w to about 90% w. The remainder of the composition may comprise an excipient glass former with additives included as needed. For most compositions, additives will be present in the matrix at a level of less than about 20% w.

(*Id.* at ¶ [0079].)

Analysis

We agree with Appellants that the Examiner has not adequately explained why it would have been obvious to include leucine in an amount of from about 62 to about 82 weight percent. In particular, given the disclosure that,"[f]or most compositions, additives will be present in the matrix at a level of less than about 20% w" (FF 26), we do not agree with

the Examiner that including about 62 to about 82 weight percent leucine constitutes mere optimization.

Conclusion

The Examiner has not set forth a prima facie case that the applied references suggest particles comprising about 62 to about 82 weight percent leucine. We therefore reverse the obviousness rejection of claims 172 and 173.

SUMMARY

We affirm the obviousness rejections of claims 140-143, 153, and 156-170 over Tarara in view of Slutsky, alone or further in view of PDR or Warren. However, we reverse the obviousness rejections of claims 140-143, 146-150, 159, 160, 162, 172, and 173 over Foster in view of Tarara and Slutsky, alone or further in view of DIH. Thus, claims 146-150, 172, and 173, as well as claim 171, are not currently subject to a rejection.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

alw

ELMORE PATENT LAW GROUP, PC
515 Groton Road
Unit 1R
Westford, MA 01886